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Serologic Patterns in Syphilis

By
John C. Cutler, M. D.
Leader "WHO", Venereal Diseases Control Team,
Hawthorn Cottage Simla.

With the discovery of the effectiveness of penicillin in the cure of syphilis, new interest has been taken in the serologic response of the patient to treatment and a greater appreciation of the meaning of serologic changes in the treated disease has developed. It is the purpose of this paper to discuss the serologic changes observed in penicillin-treated syphilis before, during, and after therapy as reflected by the battery of standard serologic tests for syphilis performed on blood samples drawn at frequent intervals.

Certain of the information presented is based upon the results of quantitative testing without which it is impossible to follow satisfactorily a treated case of syphilis. The exact techniques of the tests used in these records are described by the author serologists (1) Here it is sufficient to say that the technique of quantitation involves the testing of serially diluted specimens of serum in order to determine the dilution in which the end point of activity is found. In essence, the information obtained is similar to that found by titration of serum in the Widal or related procedures. In the records presented in this paper, each separate figure in the columns headed "Mazzini" and "Kahn", Quantitative Methods, represents the reaction in the serially diluted tube and is read from left to right. If we use record 2, we find that at 0 days the first 4 Mazzini or Kahn represents the reaction obtained in the undiluted serum; the next 4 the reaction in dilution of 1 : 2; reactions in the dilutions of 1:4, 1:8, 1:16, etc. follow. As the reaction becomes stronger or weaker, positive results are obtained in sera with greater or lesser dilution. Thus it is evident how the strength of reaction in a given serum, or the titre of the serum, is measured.

It should be noted that some authors report the results of tests in terms of units. In general it can be said that as the number denoting units increases, the dilution in which the serum is positive becomes greater and vice versa. The interpretation of the unitages reported for any test must be based on a knowledge of the technique used in that particular test. However when the results of quantitative testing are shown in each of the serial dilutions as in the accompanying records, the appreciation of changes in titre is not difficult.

Through the kindness of Dr. R. C Arnold, director of the Venereal Disease Research Laboratory of the United States Public Health Service, the serologic records of some of the patients treated in his clinic were made available as types to illustrate the discussion of the serologic changes observed in syphilis. Blood samples were drawn from the patients at regular intervals during and after treatment of syphilis by penicillin alone. The figures in the column headed "time after start of therepy" indicate the time in days and months after the beginning of treatment which is shown as 0 days. A negative figure indicates so many days before beginning of treatment. The horizontal line seen in the column indicates that treatment was completed on the day indicated by the figure above the line. Each sample was subjected to a battery of serologic tests for syphilis as shown. The tests were performed according to the technique of the author serologists (1).

It will be noted that records No. 4, 5, 6, & 7 show only three qualitative and one quantitative test. They have been purposely shown to demonstrate the fact that in order to follow a treated patient in a completely satisfactory fashion it is not necessary to have recourse to a large battery of tests with several different quantitative procedures. It is a fact that, for practical purposes, and especially when laboratory facilities are limited, the patient can be followed in a completly satisfactory fashion by one single test procedures which is quantitated.

After infection with T. Pallidum, the disease enters an incubation period which may be as long as 120 days but is usually three to six weeks after which a primary chancre develops at the site of invasion. When the chancre appears, the blood is usually negative to all of the standard serologic tests. Within two to three weeks changes take place in the serum which are reflected in the reaction of the serologic tests ; that is, the blood becomes positive. The level of sensitivity of the standard reactions used in the U. S. A. is such that, in general, the commonly used diagnostic tests can be said to be approximately equal in sensitivity. The exclusion tests are set at a higher level of sensitivity (with a consequent loss of specificity.) Thus it might be expected that the exclusion tests

would show a positive reaction before the diagnostic tests do so. However, there are individual patterns of response to infection as shown in Records 1, 2 and 3 in which the so-called supersensitive Kline exclusion test was only weakly positive or negative while various other of the diagnostic tests showed reactivity earlier in the course of the disease, or more strongly. This serves to emphasize the fact that an individual pattern of entrance to the sero-positive state does exist as shown by the response of the individual tests by a battery of tests while entering the seropositive state. While this is of theoretical and academic importance, it is not of great significance with respect to the management of the individual patient. For, usually within one week and almost always within two weeks of the time that the first positive or weak positive reaction appears, all of the tests of the battery used in the cases shown will have turned positive. Not infrequently a change from negative to positive reaction by a given procedure will take place in one or two days (2). The possible variations should be appreciated, but not overestimated. For in the management of the individual case when only one or two serologic procedures are available the patient will certainly be kept under observation by repeated examinations until a definite diagnosis can be made, if the serologic test and darkfield examination are negative upon the first examination. For no one with a knowledge of venereal disease will dismiss a patient with a genital ulcer as non-syphilitic on the basis of a single negative test. Thus the differences in time of entrance seropositivity as shown by different tests are not of great importance with respect to management of the individual patient. What is important is securing quantitation and understanding the behaviour of the procedure used.

Once the patient has entered the sero-positive stage as shown by any one reaction, all the others very rapidly become positive if treatment is withheld. But even if treatment is started in the sero-negative or early sero-positive stage the changes which take place during the first week after treatment are similar to those observed in untreated syphilis and show an increase in strength of sero-positivity as shown in Records 1, 2, 3, 4 and 7. When treatment is withheld for longer periods, the strength of sero-positivity reaches a maximum and then falls to a lower level. As the disease progresses, from time to time there may be observed increases in titre of the serum which may or may not be related to activity of the syphilitic process.

But when adequate treatment is given a favourable response is shown by a fall in strength of serologic reaction as revealed by quantitative testing (Records 1, 2, 3, 4, 5 and 7).

With respect to speed of serologic reversal, the following general statements can be made :

1. Cases of primary syphilis become sero-negative earlier than those of secondary syphilis.

2. The higher the serologic titre at onset of treatment the longer will be the time required for reversal.

3. In general, a satisfactory response to treatment is shown by return to sero-negativity or a low serologic titre within less than twelve months after treatment (3) (4) (5).

Reference to the serologic records shown in this report will demonstrate that the serologic titre of the individual serum as measured by several different techniques is a function of each separate technique. For instance, in Record 1, eight day after start of therapy, the highest dilution in which any activity was shown by the Mazzini, Kahn, and Kolmer test was 1:32, 1:16, and 1:16 respectively. The quantitative differences in height of titre as shown by subjecting a given sample to two different procedures are not clinically significant, for the pattern of increasing or decreasing titre follows in general the same basic curve in spite of individual variations in test procedure or patient, so that the differences in titres observed by different quantitative tests are functions of the tests and patient and are not necessarily indicative of the course or stage of the disease. Here it may again be pointed out that a patient may be satisfactorily followed by the use of a single quantitative method as shown by Records 4, 5, 6, and 7. While the use of several quantitative tests is interesting as a research measure, it is not necessary or advisable as a routine procedure.

As a patient approaches sero-negativity the time interval at which the various tests become negative is again determined both by the individual and the test procedures used. In general, and with reference to the battery of tests shown in the records given here, it can be said that the Kline Exclusion and Mazzini tests usually continue to show doubtful reactions for a variable period after the others have become negative. However, in individual cases any one or several tests may continue to give consistantly or erratically positive results in low titre or weak positive reactions for long periods of time even for years after successful therapy. There is reason to believe that a few individuals who have persistant positive serologic tests in a low titre by one or more procedures in the face of sero-negativity by all the others are those who would have been found to show the same false positive pattern before infection. A number of such cases are found in the records of the Venereal Disease Research Laboratory of the United States Public Health Service (2). The persistance of or sporadic occurrence of sero-positivity in low titre for a long period of time after therapy is of no significance and is not an indication of need for retreatment.

Records 1, 2, 3, 4, and 5 show some of the various patterns of entrance into sero-negativity. Records 1, 2 and 4 show the sporadic occurrence of weak reactions by one or more procedures which can some times be explained by the presence of intercurrent, unrelated infections such as virus pneumonia or other infections which are known sometimes to cause false positive reactions. However, in many cases no basis for this phenomenon can be demonstrated. It is perhaps worth mentioning that the pattern of satisfactory response to penicillin therapy shows no significant varions with different schedules or penicillin preparations.

The need for retreatment is indicated by serologic findings alone if no clinical evidence of re-infection or relapse presents first. In primary and secondary syphilis sero-failure is indicated when the blood does not show a significant fall in titre within less than twelve months after therapy. Sero-relapse is demonstrated by a significant fall followed by a significant rise in serologic titre. It should be pointed out that in treatment failure the serologic evidence is apparent before the clinical evidence is shown (4) (5) (6). However, a certain proportion of patients with sero-failure will not present clinical manifestations. The typical pattern of relapse is shown in record 6 in which there was satisfactory response to retreatment by penicillin alone. Relapses, when they occur, will almost always appear during the first year following treatment according to the opinion of many authors, (2), (6). The appearance of a so-called relapse after the first year post-treatment usually represents re-infection (6). In contrast to relapse in a patient who has reached seronegativity, re-infection in such a patient is shown by the development of a lesion followed by serologic changes. Re-infection is possible in a patient who has not reached sero-negativity (2) and in such cases the serologic changes observed are of no real help in distinguishing between relapse and re-infection. It should be noted that asymptomatic reinfection is possible in which case the serologic pattern may be that of sero-relapse or sero-failure (6).

The serologic pattern in treated latent syphilis is not demonstrated by a record, but can be summarized by saying that seroresistance is to be expected in the average case of latent syphilis of over five years duration even if given adequate therapy (7). In this stage satisfactory progress is indicated simply by the absence of a significant increase in sero-positivity or clinical evidence of progress even though the blood does not become negative. It is of course evident that without quantitative testing the status of such a patient cannot be satisfactorily assessed.

In summary, the following statements can be made with respect to the serologic patterns of early and latent syphilis:

> From inspection of the serologic records given here it is evident that a case of treated syphilis cannot be satisfactorily followed without the performance of quantitative serologic tests.

The pattern of entrance into and exit from the sero positive state is a function of the individual, the duration and stage of the disease, and the procedure used.

As long as quantitative testing is performed, any one of the standard serologic tests for syphilis can ordinarily be expected to give the information necessary to indicate the progress of the patient.

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TABLE I

RESULTS OF SEROLOGY

Case 10-J. R.-Number 122935 *Duration of Disease—21 Days*

Time after start of therapy	QUALITATIVE METHODS							QUANTITATIVE METHODS		
	Supersens	Diagnostic Flocculation					Comp Fix	Diagnostic Flocculation		Comp Fix
	Kline Rect	Mazzini	Kline Diag	Kahn Stand	Hinton	Eagle	Kolmer Simp	Mazzini	Kahn	Kolmer
Days										
0	3Dbt	1Dbt	—	—	Pos	—	—	111.....	.....	....
1	1Dbt	3	—	2	Pos	—	—	3321.....	28.....	....
3	1Dbt	3	—	2	Pos	Pos	3	3321.....	28.....	344328...
8	4	4	4	4	Pos	Pos	4	443228	4428	44444.....
14	4	4	4	4	Pos	Pos	4	44432	4428.....	444432...
20	4	4	1Dbt	4	Pos	Pos	3Dbt	44321.....	438.....	3311.....
28	2	4	3Dbt	3	Pos	—	3Dbt	43211.....	433.....	2233.....
35	1Dbt	2Dbt	3Dbt	1Dbt	Pos	—	—	2211	33.....	....
42	3Dbt	2Dbt	—	—	Pos	—	3Dbt	211	1.....	23.....
49	3Dbt	—	—	—	—	—	—	.....	.....	.....
56	3Dbt	1Dbt	—	—	—	—	—	1.....	.....	.....333..
63	—	1Dbt	—	—	—	—	—	1.....	.....	.....
70	—	1Dbt	—	—	—	—	—	1.....	.....	.....
77	—	1Dbt	—	—	—	—	—	1.....	.....	.....
85	—	—	—	—	—	—	—	.....	.....	....
91	—	—	—	—	—	—	—	.....	.....	333
Months 4	—	—	—	—	Dbt	—	—			

3 = +

TABLE II

SPECIFIC SEROLOGIC REACTION

Primary Syphilis - Normal Decrease in Reactivity - LW

Time after start of therapy	QUALITATIVE METHODS							QUANTITATIVE METHODS	
	Supernatant	Diagnostic Flocculation					Complement Fixation	Diagnostic Flocculation	
	Kline Excl	Massini	Kline Diag	Kahn Std	Hinton	Eagle	Kolmer Simp	Massini	Kahn
Days									
0	-	4	-	4	Pos	Pos	4	44421	44429
1	-	4	-	4	Pos	Pos	4	44421	44428
9	4	4	4	4	Pos	Pos	4	44442	44441
23	-	4	-	3	Pos	Pos	4	432	441
30	4	4	3	3	Pos	-	4	4442	4431
37	4	4	1Dbt	3	Dbt	-	3	4421	41
44	3	4	-	1Dbt	-	-	4	432	48
51	1Dbt	4	-	-	-	-	4	42	1
58	1Dbt	4	-	-	-	-	-	43	1
65	2	2Dbt	-	-	-	-	-	21	
72	1Dbt	2Dbt	-	-	-	-	-	21	
80	-	2Dbt	-	-		-	-	28	3
96	-	2Dbt	-	-	-	-	-	2	
93	-	1Dbt	-	-	-	-	-	1	
101	8Dbt	1Dbt	-	-	-	-	-	1	
108	8Dbt	1Dbt	-	-	-	-	-	1	
114	-	1Dbt	-	-	-	-	-		
121	-	-	-	-	-	-	-		
128	8Dbt	-	-	-	-	-	-		
142	-	-	-	-	-	-	-		
149	-	-	-	-	-	-	-		
156	-	-	-	-	-	-	-		
164	-	-	-	-	-	-	-		
177	-	1Dbt	-	-	-	-	-		
191	-	-	-	-		-	-		
205	-	-	-	-	-	-	-		
220	-	-	-	-			-		
233	-	-	-	-	-	-	-		
260	-	-	-	-		-	-		
318	-	1Dbt	-	-	-	-	-		
348	8Dbt	-	-	-	-	-	-		
450	-	-	-	-	-	-	-		
464	-	-	-	-	-	-	-		
529	-	-	-	-	-	-	-		
794	-	-	-	-	-	-	-		
812	-	-	-	-	-		-		

8 = +

TABLE III

RESULTS OF SEROLOGY

Case 29 - C.H.- Number 124684 *Duration of Disease - 15 Days*

Time after start of therapy	QUALITATIVE METHODS							QUANTITATIVE METHODS		
	Supernate	Diagnostic Flocculation					Comp Fix	Diagnostic Flocculation		Comp Fix
	Kline Eastl	Mazzini	Kline Diag	Kahn Stand	Hinton	Eagle	Kolmer Simp	Mazzini	Kahn	Kolmer
Days										
0	—	—	—	—	—	—	—			
1	—	—	—	—	—	—	—			
7	8Dbt	4	—	—	—	—	—	4321		
8	—	3	—	—	—	—	—	332		
14	—	2Dbt	—	—	—	—	—	221		
20	—	1Dbt	—	—	—	—	—	1		
28	—	1Dbt	—	—	—	—	—	1		
35	—	—	—	—	—	—	—			
50	—	—	—	—	—	—	—			

S = +

TABLE IV

W. J. - Primary Syphilis - 8 Days

	QUALITATIVE			KAHN QUANTITATIVE							
				Serum Dilutions One To							
Days	Mazzini	Kahn	Kolmer	S	2	4	8	16	32	64	128
-1	4	4	4	P	P	P	P	P	P	P	
8	4	4	4	P	P	P	P	P	P	P	P
12	4	4	4	P	P	P	P	P	P		
26	4	4	4	P	P	P	P	P	P		
61	4	4	4	P	P	P	P				
75	4	4	4	P	P	P					
96	4	1D	4								
104	3	-	4								
131	3	-	2								
164	2D	-	8D								
216	1D	-	-								
285	1D	-	-								
320	-	-	-								
361	1D	-	-								
368	-	-	-								
377	1D	-	-								

S = +

TABLE V

E. D. R. – Secondary Syphilis – 3 Days

Days	QUALITATIVE Mazzini	Kahn	Kolmer	KAHN QUANTITATIVE Serum Dilutions One To S	2	4	8	16	32	64	128
0	4	4	4	P	P	P	P	P	P	P	P
8	4	4	4	P	P	P	P	P	P	P	
22	4	4	4	P	P	P	P	P	P		
50	4	4	4	P	P	P	P				
84	4	4	4	P	P	P	P	P			
91	4	4	4	P	P	P	P	P			
114	4	4	4	P	P	P	P				
142	4	4	4	P	P						
167	4	3	2								
181	3	2	1								
217	2D	-	1								
246	1D	8D	-								
348	1D	-	8D								
390	1D	-	-								
437	-	-	-								
496	-	-	A.C.								

S = ±

TABLE VI

J. M. – Primary Syphilis – 27 Days

Days	QUALITATIVE Mazzini	Kahn	Kolmer	KAHN QUANTITATIVE Serum Dilutions One To S	2	4	8	16	32	64	128
0	4	4	4	P	P	P	P	P	P		
8	4	4	4	P	P	P	P	P	P		
21	4	4	4	P	P	P	P				
35	4	4	4	P	P	P	P				
49	4	4	4	P	P						
63	4	2	4	P	P						
77	4	2	4	P							
91	4	8D	1	P							
112	3	-	1								
140	3	1D	4								
154	4	4	4	P	P						
168	4	4	4	P	P	P	P				
182	4	4	4	P	P	P	P				
201	4	4	4	P	P	P	P	P			
217	4	4	4	P	P	P					
231	4	3	4								
252	4	2	4								
301	-	-	4								
322	2D	-	1								
385	1D	-	-								
420	1D	-	-								
467	1D	-	-								
476	-	-	-								
532	-	-	-								
595	-	-	-								
608	-	-	-								

S = +

TABLE VII

J. P. B. - Primary Syphilis - 21 Days.

	QUALITATIVE			KAHN QUANTITATIVE							
				Serum Dilutions One To							
Days	Mazzini	Kahn	Kolmer	5	2	4	8	16	32	64	128
0	1D	-	-								
8	4	4	4	P	P	P					
20	4	4	±D	P	P						
35	2D	1D	-	P							
42	2D	-	±D								
56	1D	-	-								
70	1D	-	-								
91	-	-	-								
99	1D	-	-								
119	-	-	-								
154	-	-	-								
193	-	-	-								
251	-	-	-								
316	-	-	-								

D = ±

TABLE VIII

NONSPECIFIC SEROLOGIC REACTION

B.D.C - Fungus Infection

Date	Kline Excl.	Mazzini Floc.	Kline Diag	Kahn Std.	Hinton Floc	Eagle Floc.	Kolmer C.F.
8-22	-	1Dbt	-	4+	Dbt	Dbt	-
9-6	-	1Dbt	-	1Dbt	Dbt	-	-
9-20	-	1Dbt	-	1Dbt	Pos	-	-
9-28	-	1Dbt	-	-	-	-	-
10-2	-	-	-	2+	-	-	-
10-24	2+	-	±Dbt	±Dbt	Dbt	Dbt	-
11-10	-	-	-	-	-	-	-
11-13	-	-	-	-	-	-	-
11-29	-	-	-	-	-	-	-
12-14	-	-	-	-	-	-	-

D = ±

TABLE IX

NONSPECIFIC SEROLOGIC REACTION

J. B. - No Diagnosis

Date	Kline Excl.	Mazzini Floc.	Kline Diag	Kahn Std.	Hinton Floc	Eagle Floc	Kolmer C. F.	Mazzini Quant
1-25	4+	4+	4+	2+	—	—	—	42.....
1-27	1Dbt	1Dbt	2+	—	—	—	—	
1-29	4+	4+	4+	—	—	—	—	4321...
1-30	3+	3+	2+	—	—	—	—	
1-31	2+	4+	±Dbt	—	—	—	—	
2-2	4+	4+	2+	—	—	—	—	41.....
2-5	4+	4+	2+	—	—	—	—	42.....
2-21		2Dbt		—	—	—	—	
2-28	3+	3+	1Dbt	—	—	—	—	
3-27	4+	4+	2+	—	—	—	—	41.....
4-7	3+	3+	1Dbt	—	—	—	—	
4-17	1Dbt	4+	±Dbt	—	—	—	—	
5-9	—	2Dbt	—	—	—	—	—	

D = ±

TABLE X

R. B. - NO DIAGNOSIS

Date	Kline Excl	Mazzini Floc.	Kline Diag.	Kahn Std.	Hinton Floc.	Eagle Floc.	Kolmer C. F.
10-25	—	1 Dbt.	—	1 Dbt.	Dbt.	Dbt.	—
10-30	—	1 Dbt.	—	—	—	Dbt.	—
11-9	3 Dbt.	1 Dbt.	—	3 Neg.	Pos.	Pos.	—
11-15	QNS	1 Dbt.	QNS	1 Dbt.	Dbt.	Dbt.	—
11-27	3 Dbt.	1 Dbt.	—	—	Dbt.	Dbt.	—
12-13	3 Dbt.	1 Dbt.	—	3+	Pos.	Dbt.	—
12-20	1 Dbt.	1 Dbt.	—	1 Dbt.	Pos.	Pos.	—
1-2	—	1 Dbt.	—	—	Pos.	Dbt.	—
1-9	—	1 Dbt.	—	1 Dbt.	Dbt.	Dbt.	—
1-23	1 Dbt.	1 Dbt.	—	—	Pos.	Dbt.	3 Dbt.
3-5	1 Dbt.	2 Dbt.	—	—	Dbt.	Pos.	—
3-14	3 Dbt.	3+	—	—	—	Dbt.	—
6-5	—	—	—	—	—	—	—

3 = ±

TABLE XI

M. J. McC. - NO DIAGNOSIS

Date	Kline Excl	Mazzini Floc	Kline Diag.	Kahn Std.	Hinton Floc.	Eagle Floc.	Kolmer C. F.
12-6	4+	1 Dbt.	2+	—	—	—	—
12-7	4+	2 Dbt.	2+	—	—	—	—
12-10	2+	2 Dbt.	1 Dbt.	3 Neg.	—	—	—
12-18	2+	1 Dbt.	—	—	—	—	—
1-3	—	—	—	—	—	—	—
1-18	—	—	—	—	—	—	—
1-31	—	—	—	—	—	—	—
4-19	—	—	—	—	—	—	—

3 = ±

Cutaneous Manifestations of the Hereditary Hemolytic Anemias

By

Samuel M. Bluefarb, M. D.

Assistant Professor of Dermatology,

Northwestern University Medical School, U. S. A.

The hereditary hemolytic anemias are ; congenital hemolytic jaundice, sickle cell anemia and Mediterranean target-oval cell anemia (Cooley's anemia).

Congenital Hemolytic Jaundice

A hereditary defect of the "erythron" is accepted by most authors as the cause of congenital spherocytic hemolytic jaundice. The disease is a dominant hereditary property and the underlying change in the genotype appears to rest with a single gene (1).

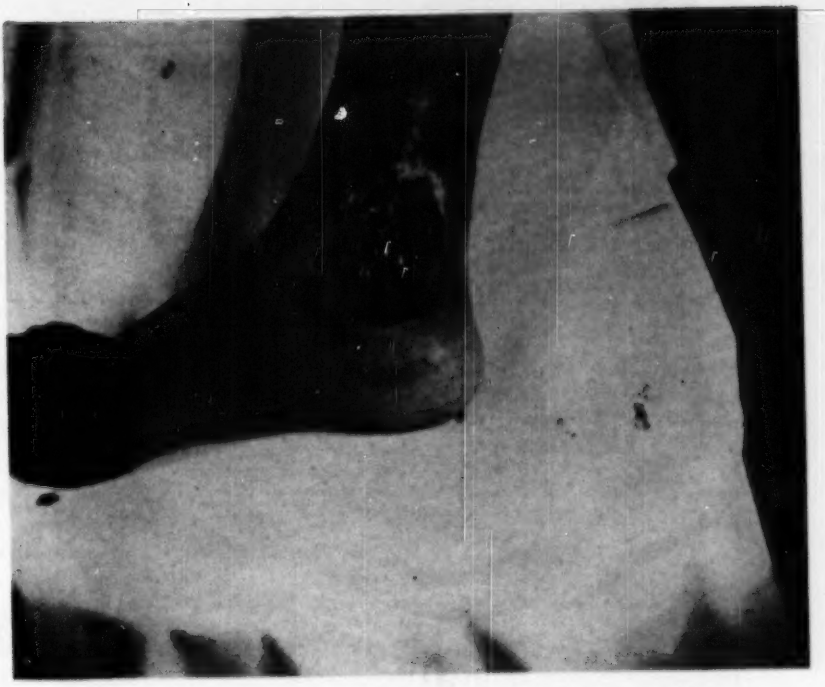
Jaundice : Jaundice is the usual presenting manifestation of the malady (2). It may be apparent at birth, in childhood or, occasionally, not until adult life. It fluctuates widely in intensity, but is rarely more than moderate in extent. The skin of the body may show a marked lemon-yellow colour, but the face is usually buff-coloured. The greenish colour of deep, longstanding jaundice is never present. The condition is not associated with toxemia, pruritus, bradycardia or hemorrhagic tendency. The intensity of the jaundice is not dependent on the degree of anemia, but is related to three factors : (1) The degree of fragility of the erythrocytes, (2) the activity of the spleen and (3) the biliary excretion function of the liver.

Ulcers of the Legs : Ulcers of the legs associated with this anemia have been reported by various authors. The ulcers were localized on the lower portion of the leg and were strikingly persistent and refractory to any treatment excepting splenomegaly.

The great majority of patients have been young women in the second and third decades of life who gave a history of having had persistent or recurrent ulceration of the lower leg of two months to twenty years duration. The ulcers were most frequently located in the region of the medial malleolus. Usually only a single ulcer is present, but bilateral involvement is reported in about one-half of the cases. Trauma may or may not precede the appearance of the ulcer. A dusky blue area in the region of the medial malleolus frequently is the first manifestation of the ulcer. This breaks down in the center and a shallow indolent erosion

From the Department of Dermatology, Northwestern University Medical School, Chicago, Illinois, U. S. A., Edward A. Oliver, M. D., Chairman.

Fig. 1



Ulcer of the leg associated with congenital hemolytic jaundice

Fig. 2.

Ulcer of the leg associated with sicklecell anemia.

occurs which advances to about 3.5 cm. in diameter. Larger punched out lesions appear only in cases of very long standing. The edges are only slightly elevated and there is little undermining. A ring of bluish cyanosis or dark pigmentation circumscribes the lesion. There is often considerable pain and, although limitation of motion is unusual, weight bearing may be considerably compromised (3).

On histologic examination the base of the ulcer is usually found to be hemorrhagic. There is an infiltration of lymphocytes and plasma cells and a few eosinophils, particularly about the blood vessels. Some of the arteries show thickening of the walls; others show hyaline degeneration. Phagocytes containing blood pigment are present. The histological picture is that of a chronic ulcer and is not specific (4).

Purpura : Purpura is frequently seen in association with congenital hemolytic jaundice.

Case Report

A 19 year old white girl first noticed a lesion on the lateral aspect of the lower third of the left leg. The lesion responded to treatment in one month, but six months later an ulcer reappeared at the same site and necessitated hospitalization for one year. One month after discharge from the hospital the ulcer again broke down and has since continued to drain. Eight months later she developed an ulcer over the medial malleolus of the right ankle following the scratching of mosquito bites.

The general medical examination was essentially negative and the past history was not significant, nor was there any history of the ingestion of drugs. Hematological diagnosis was typical congenital anemia with leg ulcers.

Physical examination disclosed a poorly developed, thin, pale, white girl who appeared to be of low mentality. She had pediculosis capitis of long duration. There was no lymphadenopathy and the spleen and liver were not palpable. The breasts, external and internal genitalia were under-developed. The axillary and pubic hair was scant and there was bossing of the skull with unusual facies, similar to that seen in congenital ectodermal defect. There were two ulcers on the right ankle : the larger 6 by 6 cm. and the smaller 3 by 2 cms. in diameter.

Please see *Figure 1.*

Laboratory Studies :

Urinalysis :

Albumin.....negative
Glucose.....negative
Microscopic.....negative

Serology :

Blood (Kahn).....negative

Blood Count :

Hemoglobin.....77 per cent.
Red Blood Cells.....3,640,000 per. cu. mm.
White Blood Cells...6,850 per. cu. mm.

Differential White Blood Count :

Polymorphonuclears .....70 per cent.
Eosinophils..... 6 per cent
Basophils ..... 0 per cent
Lymphocytes.....18 per cent
Monocytes ..... 6 per cent

Anisocytosis ..... 4 plus
Poikilocytosis ..... 2 plus
Macrocytosis..... 1 plus

Blood platelets..... 738,000 per cu. mm.
Sedimentation rate..... 36 mm/one hour (corrected)
Hematocrit ..... 36 cc. per 100 cc. of blood
(·36 volume %)

Blood Chemistry :

Total proteins .....6 5 gm. per 100 cc. of serum
Inorganic phosphorus .....4.2 mgm. per 100 cc. of serum
Total cholesterol .....157 mgm. per 100 cc. of serum
Alkaline phosphatase ..... 22 units (Bodensky units)
Icterus index 8
Cephalin flocculation 0
Thymol turbidity ..... 5.4 units

Chest X-ray :

Heart.....negative
Lungs .....negative

Sickle Cell Anemia

This condition was first described by Herrick (5) in 1910. The anemia is familial and apparently hereditary, dominant in character, and transmitted according to the Mendelian law.

The disease usually occurs in persons with Negro blood although it has been reported in white person of Syrian, Sicilian, Greek and Mexican stock. The condition is characterized by the peculiar sickle or oat shape which the erythrocytes assume in fresh blood preparations.

The essential pathological changes have been summarized by Diggs and Ching (6) as follows: sickled erythrocytes, congestion of the capillaries, thrombi, infarcts, fibrosis, hemolytic anemia with increased phagocytic activity of the reticuloendothelial system, retention jaundice, deposits of pigment in the liver, spleen, bone marrow, lymph nodes and kidney, hyperplasia of the bone marrow, a regenerative blood picture and degenerative visceral changes. Diggs and Bibb (7), having found the small blood vessels distended by sickled cells, advanced the theory that the great length of these cells interferes with the free circulation of the blood and that this is a factor in the production of thrombosis, a common feature in this disease.

Murphy and Shapiro (8) are of the opinion that no evidence has yet been advanced that the clinical manifestations are due to any cause other than vascular occlusions on the basis of mechanical obstruction and thrombosis. The essential pathologic process in sickle cell anemia is the stagnation and conglutination of disfigured red corpuscles.

The following signs and symptoms are listed in order of frequency by Anderson and Ware (9): greenish yellow scleras, heart murmurs, enlargement of the liver, adenopathy, abdominal pain, enlarged heart, ulcers of the leg, pulmonary disease, fever, enlarged spleen, vomiting and infantile genitalia.

The yellow sclera is believed by Mc Gavack and Nussbaum (10) to be common clinical manifestation and uniformly associated with an increased icteric index. The colour of the eyeball is to be distinguished from the frank yellow colour seen in biliary jaundice and from the muddy pigmentation of the fatty-like deposits frequently seen in normal negroes.

Ulcers of the legs are more commonly seen in sickle cell anemia than in any other form of anemia. Chronic ulcers or scars of old ulcers are present in 75 per cent of adults with this disease. Cummer and La Rocco (11) state that an impressive fact is the phrase "punched out" invariably used in descriptions of these ulcers. The ulcer may be single or unilateral, but multiple and bilateral ulcers have been reported. The most frequent location is in the neighborhood of the ankle, but any part of the leg may be involved. The size of the ulcer ranges from one to seven cms., or larger, in diameter. It is usually sharply marginated, round or oval, and may be shallow or deep, with elevated and irregular borders. The base usually shows granulation tissue and is occasionally suppurating or, in some instances, covered with dried serous or sero-purulent crusts. The appearance may be that of ecthyma. The resulting scars are atrophic, glossy, smooth, depigmented and usually surrounded by a pigmented border or areola. Microscopically there is moderate increase in connective tissue with an

increase in plasma, mononuclear, lymphoid cells and some neutrophilic polymorphonuclear infiltration. The base of the ulcer is composed of granulation tissue possessing no characteristic suggestive of any specific etiology. The blood vessels show endothelial proliferative and obliteral changes in the arteries. Capillary and venous thrombosis may be present.

Other skin manifestations that may be presented with sickle cell anemia are: increased pigmentation at points of trauma (10), vitiligo, multiple subcutaneous swellings, and pseudo-ophiasis (12).

Case Report

A 26 year old negro labourer presented an ulcer of the medial aspect of the right ankle of eight years' duration. Four years after the onset the patient was treated with red blood cell paste applied to the ulcer twice a day. The lesion healed after six months of treatment and did not recur until four years later when the ulcer reappeared in the same area.

Past history revealed a recent attack of "yellow jaundice" which the medical consultant regarded as a superimposed infectious hepatitis. The history did not reveal any other member of the family having sickle cell anemia or the sickle cell trait.

Physical examination showed the heart and lungs to be normal. There was no enlargement of the spleen or liver. A superficial, irregular, moderately tender ulcer, measuring 1.5 by 2.5 cms. in diameter, was present on the medial aspect of the left ankle.

Please see *Figure 2*.

Laboratory Studies:

Urinalysis:

Albumin.....negative
Glucose.....negative
Microscopic.....negative

Serology:

Blood (Kahn).....negative

Blood Count:

Hemoglobin.....70 per cent
Red Blood Cells.....4,100,000 per cu. mm. (with active sickling)
White Blood Cells.....8,200 per cu. mm.

Blood Chemistry:

Total Protein.....6.7 gm. per 100 cc. of serum
Icterus index.....14
Thymol turbidity.....3.1 units
Cephalin flocculation...0
Chest X-Ray:.....Normal

Cooley's Anemia

Cooley and Lee (13) first described Mediterranean disease (thalassanemia) in 1925. It is generally recognized as a distinct entity characterized by hemolytic anemia, enlargement of the spleen, the presence of large number of nucleated red blood cells in the peripheral blood, changes in the bones and familial and racial incidence.

Smith (14) states that in advanced cases of Mediterranean anemia the skin and facies present a striking diagnostic appearance. The pale, muddy yellow pigmentation of the skin and mongoloid facies produced by changes in the skull bones are characteristic. The increasing pallor in some instances is replaced by a dark pigmentation of the skin which, during the terminal stage, assumes an aspect of bronzing. Whipple and Bradford (15) studied the deposition of iron containing pigment in the organ of patients who died of Mediterranean anemia. They considered this pigment to be as characteristic of the disease as is any other finding. It resembles that seen in hemochromatosis.

Ulceration of the skin of the legs may occur in Mediterranean disease. Such ulceration cannot be distinguished grossly from that occurring in sickle cell anemia and congenital hemolytic icterus. Histologic examination of an ulcer showed the prominent deposition of iron in the cutis to be an outstanding feature.

Three adult patients with Mediterranean anemia were studied at the Mayo Clinic (16). The patients were sisters of Italian descent all of whom, at one time or another, had ulcers of the legs. Histologic examination of skin from the border of one of these ulcers was performed on a 23 year old patient in this group. The epidermal changes consisted of minimal hyperkeratosis and irregular acanthosis. In the upper half of the cutis the capillaries and arterioles were increased in size and number and there was moderate infiltration of lymphocytes, connective tissue cells, chromatophores and polymorphonuclear leucocytes. In the mid-portion of the cutis there were several areas of beginning necrosis with disintegration of cells, so that recognition of cell types in these areas was not possible. Elastic tissue was absent throughout the upper portion of the cutis, and very little elastic tissue was present in the vessels. Degenerative changes, homogenization of collagen and moderate edema were seen in the arteriolar walls. Dense deposits of iron seen in the midportion and lower portions of the cutis stained with ferric thiocyanide.

Summary

The common cutaneous manifestations of hereditary hemolytic anemias are jaundice, ulcers of the legs and purpura.

The less commonly observed manifestations are pigmentation, vitiligo, subcutaneous swellings and pseudo-ophiasis

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Psoriasis

By

M. C. Rama Ayyangar, B.A., M.B. B.S.,

Civil Assistant Surgeon, Tellicherry.

—:o:—

Psoriasis is a non-infectious chronic intractable skin disease characterised by the presence of copious silvery scales set on erythematous raised papules which gradually increase in size to form irregular patches with definite margins and which occur on certain parts of the body especially the extensor aspects of limbs, scalp and nails. This is less common in the coloured races; common in young adults, but rare in infants and aged people. There is no special predilection of either sex.

Etiology

It is varied and obscure. (1) There is a *hereditary predisposition* (in 30% cases according to Ingram) (2) Kyrle considered Psoriasis to be due to *Virus*. (3) It has been attributed to *parasitic agents* and by some others to *Fungus* (Monilia). (4) Some authors have attributed it to *Toxins of bacterial or metabolic origin*, as they found Focal sepsis or increased blood sugar content or increased blood cholesterol. (5) Some workers hold that *nervous influences* may determine an attack and that worry and anxiety may aggravate it. (6) It is considered by some to be a sort of *Allergic reaction* of skin associated with *Hormonal dysfunction* together with *Vitamin deficiency*. Dr. Lahiri (1943) found blood Vitamin content in patients with Psoriasis lowered from the normal 1.2 mgms. to 0.18 mgm. per 100 c. cm of blood. (7) Scratching (*Trauma*) may determine the site of a patch. Thus the etiology of this skin condition is by no means clear or definite. However it is possible that upon a primary hereditary predisposition one or more of the secondary factors (food, toxaemic, endocrinal or psychic) may be instrumental.

Histo - Pathology

In the corium the inter papillary processes become irregular, branched and push their way downwards between the papillae which therefore become thinned out, lengthened and extend deep down into the cutis vera. In this papillary layer there is dilatation of the capillary loops and oedema and round cell infiltration (no plasma cells) around the vessels. In the epidermis the basal layer is normal, but above it there is great exaggeration of the thickness of prickle cell layer (*Acanthosis*). Cell division which is limited normally to St. Germinativum now occurs in the St. Mucosum in which there are also signs of inflammatory reaction (i. e.) intercellular oedema which interferes with keratosis and separation widely of the prickle

cells. St. Granulosum is not formed. St. Lucidum is normal. But in St. Corneum (Horny layer) there is *Para Keratosis* (i. e) there is proliferation of the epithelial cells which retain their nuclei and which are moist, sticky and form scales. Polymorph cells migrate from the papillae through the prickle cell layer and collect in masses between the horn cells in the scales. Thus there are dry abscesses in the epidermis. The silvery appearance of the scales is due to included air.

Symptoms and Signs

Psoriasis is a chronic disease recurring often at irregular intervals (rarely seasonal). *Type of lesion.* It starts as a red papule (in dark people less red and it may vary from pale to bright red) of the size of a pin's head, spreads peripherally and becomes covered with dry silvery scales which are easily removable. The lesions are raised and dry. On treatment, when the lesions clear up, there is little or no pigmentation left behind (except in very chronic cases). In chronic treated cases the patches have a polished surface, but on scratching the scales become apparent. When the scales are removed there is a smooth glistening dry surface which shows, when viewed through a lens, numerous tiny red points, (the dilated capillary vessels in the papillary layer) *Buckley's Membrane.* Usually there is no subjective symptom, but occasionally *Itching* is present. General health is not affected. There may be increased blood sugar or blood cholesterol content.

Arrangement of lesions varies. In some they are of the size of pea (Psoriasis guttata) or larger (P. Nummulata); in some the centre clears up leaving rings (P. Circinata); in some others the rings run together to form gyrate figures (P. Gyrata) and in few other cases the lesions may be confined to the follicles (Follicular P.). In a few patients especially on scalp the crusts may be thick and the scales highly moist (P. Rupioides). Thus the lesions may be patches that assume all sorts of shape and size and may vary from papules to plaques.

Distribution is almost symmetrical. The sites of election are extensor aspects of limbs (knee, elbow), back of trunk, scalp and rarely nails, palms and soles. The mucosa are not affected. The lesions may start in the scalp and spread to the forehead; there may be extensive involvement without loss of hair. In the case of nails there may be rows of small pin head pits or the nail may become rough, thick, yellow and friable or the lesions may occur in the nail bed, forcing and breaking up the nail. In palms and soles they may occur as red patches which are symmetrical, circumscribed, thickened, and covered with scales or as deep painful fissures or as sharply defined red patches in which are imbedded minute sterile pustules. (*Pustular Psoriasis*).

Varieties of Psoriasis. Other varieties are. :—

1. *Flexural P.* The smooth red areas are without the scales and have sharp edges; affects the flexural aspects of the body.

2. *Arthropathic Psoriasis* is a severe form with associated periarthritis of the terminal phalanges of the fingers and overlying lesions of the skin and nails.

Differential Diagnosis

1. (a) *Papulo squamous Syphilides* (Secondary). The lesions are smaller than in Psoriasis, more uniform in size; the colour is deep red and when the scales are removed there is considerable infiltration; they are more common on the trunk and flexures. W. R. is positive; they respond quickly to Arsenicals.

(b) *Scaly circinate Tertiary Syphilides.* When these heal there is scarring left behind.

2. *Seborrhoeic Dermatitis.* The scales are yellow, greasy, moist flakes. The patches spread by aggregation of follicular papules. The edges of the lesions are indefinite (especially those on scalp). Usually scalp, face, centre of chest and back, flexures of limbs are affected. The lesions respond quickly to sulphur.

3. *Eczema.* The lesions are made up of aggregation of papules and papulovesicles. When scales are removed a moist surface is left behind. Itching is marked.

4. *Pityriasis Rosea.* The lesions are pale pink, small, oval patches with tiny scales and occur mostly on the trunk (limbs are rarely affected). There is itching. It never recurs.

5. *Lichen Planus.* The lesions are polygonal, flat-topped, shiny and lilac or purple coloured. The initial papules are not scaly, but the chronic ones are. Some are discrete, some coalesced to form plaques. Mostly the flexor aspects of the limbs are affected. Itching is generally intense. There are symptomless white spots and streaks on the buccal mucosa in 50% cases.

6. *Tinea Circinata.* There is a tendency to form vesicles or pustules.

Treatment

General Treatment. Rest in bed especially in acute cases. Avoid soaps while bathing.

Diet. Give more of carbohydrates, plenty of vegetables and vitamins and less of proteins, fat and salt. Rice with sour buttermilk is good. Avoid tea, coffee, cocoa and alcohol.

Treat the cause i. e., treat the *Focal Sepsis, Nervous Influences,*

Hormonal dysfunction and vitamin deficiency, by appropriate therapeutic measures. It is necessary to treat the scalp condition primarily; otherwise there is recurrence of the lesions on the body.

Internal Medication. Though there is no rationale of internal therapy a large number of medicaments are administered orally, sometimes with benefit.

(a) In acute cases in whom Arsenic is injurious and in whom there are spreading red moist spots, give orally Quinine or Soda Salicylas or Salicin in full doses (15 grains t. d. s.).

(b) *Arsenic* is the most valuable drug and is given as Liq. Arsenicalis m. 2, t. d s. increasing the dose gradually upto the limit of tolerance (m. 8 t. d. s.). It is beneficial only in chronic case and in cases where the pink spots are not spreading and are not moist. So it should not be given in acute cases or given for long periods continuously and should not be continued indefinitely when there is no therapeutic response. (c) *Mercury*. Orally it is administrated as Liq. Hyd. Perchlor 1/2 drachm t. d. s. or as Hyd. Iodidi Viridis Tabloids (B W. & Co.) one t. d. s.

(d) *Pot. Iodide* in 1/2 drachm doses three times daily is advocated by some. So it is useful to combine these and give them as the following mixture orally.

Liq. Arsenicalis	m 2 to 8
Liq. Hyd. Perchlor	m 30
Pot. Iodide	gr 30

Mist. Ferri et strychnine ad. 1 oz. t. d. s. after food.

(e) *Hormonal therapy*. Thyroid Extract in small doses (1/2 grain t. d. s.) has been advocated by Ingram (1939) and may with advantage be combined with oral doses of Arsenic. During treatment with Thyroid, as it is a potent drug, the patients must be enjoined complete rest and be under strict medical observation.

(f) *Therapy with vitamins*. Give vitamins particulary the B complex (such as Becozym (Roche) — 4 tablets daily orally) and also vitamin C (100 mgm orally daily) for a few weeks. The patches clear up in many cases. Pure Vitamin D2 (Super-concentrated) can be tried orally in the form of *Vide* – Alcoholic solution superconcentrated (Wanders) or as Davitamon D (Organon) in doses of 15 mgm (1 c. c. = 15 mgm = 6 lakhs I. U. Vit D2) thrice during the first week, 15 mgm twice during each of the next three weeks and 15 mgm once a week during the next few months. J. Charpy tried this regimen and had varied success in Psoriasis. Ceder and Zon tried another regimen (3 lakh I. U. of Vit D2 daily for a few weeks) and claim good results. It is essential to give in addition 1 to 2 pints of milk or calcium gluconate 1½ drachms daily orally.

(g) *Treatment of nervous back ground.* Bellergal (Sandoz) tablets have been found handy in patients with strong psychological background. It is an useful adjuvant

(h) *Undecylenic acid* seems to hold a great deal of promise in the treatment of Psoriasis when given orally, as Peelman (J. A. M. A. 139: 444, 1949) gave increasing doses orally in cases of chronic Psoriasis and found definite improvement. But further trials are necessary before it can be accepted as an efficient remedy.

Injection Treatment

Until specific therapy becomes available for this disease of doubtful etiology,

A., *Non specific protein shock therapy* is justified especially when the disease is refractory to other methods of treatment and when it is chronic, obstinate and severe or when it is accompanied by arthritis. It has been found to give beneficial results and so it is worth while to give it a fair trial. Its action depends upon the fact that the introduction of foreign proteins into the blood stream causes a sharp febrile reaction which is followed by gradual regression of the lesions. Only slight protein shock effect is obtained when milk or Aolan or Peptone or collosal sulphur is used. During the shock therapy the patients should have absolute rest in bed and be under continued medical attendance. It is good to remember that rarely collapse may ensue after shock therapy and that the following are contra-indications to protein shock therapy.

1. Arterio-Sclerosis, Myocardial weakness and Hyperpiesis.
2. Chronic Renal disease. 3. Diabetes 4. Acute T. B. 5. Severe Allergy. 6. Pronounced Malnutrition.

(A) The best method is to inject *T. A. B. Vaccine* (*Curative*) I. V. in gradually increasing doses of 10, 20, 50, 100, 150, 200 millions on alternate or every third day, diluted in 5 to 10 c.c. Normal saline. In 1-3 hours the patient gets a rigor followed by high fever (103° F.) which comes down in 24 hours. (2) Next best is *Aolan* (Bieredorf) starting with 1 c. cm I.M and increasing by 1/2 c.cm each time upto 5 c.c. biweekly. Else pure cow's milk, boiled well for 10-15 minutes in a water bath and then cooled can be injected, I.M. in buttock in the same doses. (3) *Peptone* 5% I. V. or 7½% solution I M. doses of 1/2 c.c. increasing by 1/4 c.c. up to 2 c.c. can also be used. (4) The same effect can also be obtained by *Oleo Sulfin*—Sulphur in oily suspension given I M. starting with ½ c.c. and later 1/2 c.c. every third day for 6-8 injections or by using *collosal sulphur* (Crookes) 0.1% 1 to 2 c.c. I.M. (Gray 1937).

(B) Auto Hemo Therapy

Injecting increasing doses of one's own blood into buttocks I M. (3, 5, 7, 10, 10, 10 c.c. and so on for 8-10 injections once in 4 days) has good scope in treatment of Psoriasis when other remedies fail.

(C) *Colloxal Mercury Sulphide* (Crookes) 1% is one of the most effective drugs 1-2 c.c. is given I.M. biweekly.

(D) *Enesol.* (Mercury Salicyl-Arsenate) injections have been used with success recently. 1-2 c.c. is given I.M. once in 3-4 days. A course of 16 injections are given and may be repeated with benefit after a rest of 15 to 30 days.

(E) *Colloxal Bismuth* 1/2-1 c. cm. I.M, biweekly for about 2 months has been found useful in some patients.

(F) In cases of Psoriasis with associated FOCAL SEPSIS, *Auto Vaccine* in small doses at intervals has been found to be a useful adjunct.

(G) In cases with an allergic basis, Antistine (Ciba) and Lertigon (P.D. & Co.) can be used with advantage. Antistine can be administered as tablets orally one b.d. along with I.M. injections of the same drug (1 amp. daily in the first week and on alternate days in the second week) and this course may be repeated after an interval. Lertigon (P. D. & Co.) is Histamine Azoprotein and has been used subcutaneously by Dr. A. V. S. Sarma with encouraging results.

(H) *Hormones.* Some claim success with Adrenal Cortex (i.e.) CORTIN. (Maddan 1940). In women Testosterone Propionate in doses of 10 mgm I. M. can be given 5-6 times between the 12th and 20th day of the cycle, as Lafitte and Huret found that in women with Dysmenorrhoea who were treated for it with Testosterone, the coexisting Psoriasis disappeared.

Local Treatment

It is the most rapidly efficacious line of treatment. If the patches are inflamed, no active treatment is done but they are best treated with Lotio Calamine or Simple Vaseline. Chrysarobin, Tar, Podophylin are the drugs par excellence.

1. *Chrysarobin* : It is best applied in chronic cases especially if extensive, as 5-10% ointment and rubbed well into patches twice daily after a warm bath and after scrubbing off the scales with soft soap and nail brush. Then the ointment is applied on lint and the body is covered with that lint during the rest of the day and night when the patient is rested in bed. Eyes ought to be taken care of; Chrysarobin should not be used if fresh lesions are still appearing. It stains linen permanently and may set up a dermatitis or Pityriasis Rubra, if applied carelessly. So instead Cignolin or Anthralin or Derobin may be used.

Cignolin (Bayer) is very efficient though costlier; it is less messy, does not soil linen, or set up conjunctivitis. It is almost a specific when applied as 1/10 to 2% ointment.

Rx Cignolin Gr½-5
Acid Salicylic Gr. 15-20
Vaseline ad dr I F. Ung.

If this treatment is carried out thoroughly for 3-4 weeks the patches do disappear. Addition of 2% carbolic acid increases the efficiency of chrysarobin and shortens the time of treatment.

Anthralin ointment (Abbott) 1,8-Dihydroxy Anthranol (C14 H10 O3) is a derivative of chrysophanic acid; less irritating and sets up little or no dermatitis, conjunctivitis or constitutional reactions or skin discoloration. It stains linen only slightly and can be used on face and scalp. It is more effective than Chrysarobin or Tar and produces involution of inveterate Psoriasis and cures it when other forms of treatment have failed (Stokes J.A.M.A. 5-1-1935). Its value in Psoriasis has been emphasised by other dermatologists also. (Unna and others). First Anthralin ointment of low strength 0.1% is applied on a small area (especially if on face) and the strength is then gradually increased if there is tolerance; in resistant cases 1% ointment is used once or twice daily and the number of applications are gradually reduced as the lesions subside. However, the application is continued for some time even after the last patch disappears. But the ointment is with held if pustular folliculitis is set up and treatment is begun with bland simple ointments.

Dovobin (Glaxo)—Brand of Dioxy Anthranol is 2-5 times more active than Chrysarobin. It is applied as 1-2% ointment along with acid salicylic 3% and Tar 5-10%.

(2) *Tar:* is the safest for Psoriasis. First the scales are scrubbed off with soft soap and nail brush during baths and then any one of the following preparations are used.

(a) *Tar Acetone.* Pix carbonis preparata dr. I in Acetone oz. I (b) Tar Dermament (P. D. & Co.) (c) Equal parts of Pix Carbonis, soft soap and Rect. Spirit. These three are used as paints or (d) *Ung. Petrolei Compositum* is better.

Liq. Carbonis deterg.
or Liq. Picis carb. dr. I
Hyd. ammon gr. 20
Acid salicylic gr. 15
Vaseline ad oz. I F. ung.

This ointment may be rubbed thoroughly into the patches every night for one week and washed off in the mornings. Chrysarobin gr. 25-30 may be in-corporated into the above ointment with advantage and better effect. Acid Salicylic being a keratolytic removes the scales.

(3) Podophyllin

In psoriasis when podophyllin is applied externally there is remission of the lesions for long periods and there is absence of irritation. A solution containing podophyllin gr. 25-35, alcohol 80 c cm and glycerin 20 c.cm is painted on and 1/2 cm around the patches every alternate day till the scales fall and the lesions subside. The centre of patches remain pigmented for some time. However, in some cases an Eczematoid dermatitis is set up but it is easily treated by cooling dressings. Further investigations are necessary to evaluate its long term effects and its real efficacy.

(4) (4) Dr. A. V. S. Sarma has used externally ol. Bouchi (from seeds of Psoralia corylifolia) with or without methyl-Salicylas 5% liberally and had beneficial results

5. Pyrogallic ointment 5–10% is useful.

Antibiotics Etc. Penicillin has not been found of any significant value in this condition. Even the topical application of Tyrothricin is of no use. But local application of Bacitricin has been found to be effective in some cases but this needs further trial and investigation. Sulphanilamide group has no beneficial action in Psoriasis either by external application or by internal medication.

U. V. Rays

Many patients respond well to Ultra Violet Ray exposure—a clean and simple procedure. It is given as General Body baths as well as in large doses to individual patches. The patches are covered with Tar Ointment over night and it is thoroughly removed away next morning before exposing to U. V. R. The scales must have been previously removed and the skin thoroughly cleansed of all grease. U. V. R. exposures are then given 3 times a week-first for two minutes, gradually increasing to 10 minutes in 26 sittings at a distance of 3" to 36". Third and fourth degree erythema are to be produced by the Ultra Violet Rays. The patients can have a bath only 24 to 48 hours after the exposure.

X-Rays effect a rapid cure in case of localised resistant patches; are useful in the treatment of Psoriasis of Nails, of palms and soles (except Pustular Type) but not for the face. The technique is 100 KV 3 Ma; F.S.D. = 30", Filter = 0.5 mm Al; 270 to 360 U are given at the rate of 45-90 U units every alternate day. Better results follow if X.rays are alternated with U.V.R. exposures. Three to four such courses are necessary.

Psoriasis of Scalp. The scalp should be treated primarily; it should be washed twice weekly with spirit soap (soft soap 2 part and industrial spirit 1part) as shampoo. Then Liq. Carb deterg. full strength of Liq. Piscis

carb in water I in 4 is rubbed into the patch daily after removing the crusts. Or (2) 1/2% Dithranol ointment or Anthralin ointment may be applied on alternate nights, alternating with the application of the following ointment.

Rx

Resorcin	Gr. 20
Acid Salicylic	Gr. 15
Hyd amm	Gr. 15
Liq. Piscis carb	M 20
Ung. Aguosum ad. oz, I	

or (3) 5—10% pyrogallic acid ointment my be used.

(4) U.V.R. Exposures and small doses of X-Rays.

(5) Hodara's ointment also is useful.

Psoriasis of Nails. The nails should be cut away, the scales removed and then an ointment containing 2% Acid Carbolic 3% Acid Salicylic and 5% Sulphur may be applied. However X-Rays are the best.

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Avitaminosis-A in Dermatology

By

K. D. Lahiri, M. D., B. S., F.D.S (London),

Lecturer in Dermatology, Calcutta National Medical Inst.

(On leave in U. K.)

Clinical Assistant in Dermatology, Glasgow University, U. K.

Deficiency diseases in man implies a lack of many nutrients and for its treatment a satisfactory intake of all the vitamins is essential, particularly large quantities of that particular vitamin, the clinical deficiency of which is most marked. It has been found that in avitaminosis-A large doses of vitamin A are required for quite a long period to have the desired effect (Lahiri, 1945). It has been recognised now that some of the skin conditions of unknown etiology get well with Vitamin A administration for a certain period and it has been my experience both in Bihar and in Bengal during the last 13 years that cases of (1) Xerodermia or dry skin are amenable to high vitamin A therapy, although they relapse when therapy is stopped. (2) Ichthyosis is a condition of dry skin where fish scales like

lesions are marked on the extremities and quite a large number of patients improve with a high dose of Vitamin A during this period (Lahiri, 1945). (3) Phrynoderma–or toad skin cases I had the chance of observing almost in an epidemic form after the Bengal famine and amongst the refugees after the partition of India and my cases were cured in 80% with vitamin A and improved in 20% with vitamin A.

(4) Bluish macular pigmentation due to avitaminosis A, I treated with liver extract in about a dozen of cases and they were cured when vitamin A in liver extract was injected to them (Lahiri, 1947 and 1948).

(5) Acne vulgaris with vitamin A alone or vitamin A with peeling paste and sometimes also with x-ray therapy. During my six months work in Glasgow I had the chance of treating a large number of cases of acne vulgaris with high doses of vitamin A. My observation for over ten years in acne vulgaris with vitamin A therapy is that all the different types of acne at all ages are amenable to vitamin A therapy and cure can be obtained in over 75% cases with vitamin A alone in high doses for a long time, 15% cases require peeling paste also and out of 10% cases only 5% require one or two doses of x-ray therapy in addition but 5% of these cases do not respond to any treatment at all.

(6) Nummular eczema–of hands and legs which disappear in summer with good food and reappear every winter does in most cases get well when treated for a long period with vitamin A along or in combination with local application I have found it a very helpful adjuvant therapy in over 80% cases of nummular eczema at all ages.

(7) Pityriasis Rubra Pilaris–In 4 of 9 cases I have had a chance to treat with vitamin A, only two cases could be followed for an average period of 16 months and it took full 6 months Vitamin A therapy in high doses to cure but the hyperkeratosis of palms and soles did not completely clear away and no relapse was seen in these cases even when without treatment for over ten months.

An almost specific action of vitamin A in acne vulgaris makes the treatment very easy for patients. Vitamin A seems to have a specific action in the epithelial tissue and the pilo sebaceous follicles. Doses of vitamin A should be 100,000 international units per day by mouth or by injection and for a minimum period of three months. Proper maintenance of vitamin A in blood is essential for a long time.

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Third Session of the Expert Committee of the W. H. O. on Venereal Infections.

Technical considerations were the principal concern of the WHO Expert Committee on Venereal Infections when it met for its third session,[1] held in Washington from 10 to 20 October 1949. The committee discussed control techniques, antibiotic therapy in syphilis and other treponematoses, serological and laboratory aspects of venereal infections, and the report of the WHO Syphilis Study Commission to the USA.

Treponematoses

Although major effort in WHO's venereal-disease programme is to be concentrated on early infectious syphilis and prenatal and infantile syphilis,

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1. The following took part in this session :

Members :

Dr. W. E. Coutts, Professor of Venereology, Chief, Department of Social Hygiene, Public Health Administration, Santiago, Chile.
Dr. R. Degos, Professeur agrege a la Faculte de Medecine de Paris, France
Dr. S. Hellerstrom, Professor of Dermato-syphilology, University of Stockholm, Sweden
Dr E. H. Hermans, Medical Director, Association for the Combating of Venereal Diseases, Rotterdam, Netherlands.
Dr. J. F. Mahoney, Chief, Laboratory of Antibiotic Research and Development, Section of Laboratory of Infectious Disease, Microbiological Institute, National of Health (US Public Health Service), Staten Island, N. Y. USA (*Chairman*)
Dr. G. L. M. Mc Elligott, Director, Venereal Disease Department, St. Mary's Hospital; Adviser in Venereal Diseases, Ministry of Health, London, United Kingdom (*Rapporteur*).
Dr. I. H. Nagi, Director, Venereal Diseases Section, Ministry of Public Health, Cairo, Egypt.
Dr. R. V. Rajam, Professor of Venereology, Government General Hospital, Madras, India, (*Vice-Chairman*)

Co-opted Consultants :

Dr. N. R. Ingraham, Chief, Division of Venereal Disease Control, Department of Public Health, Philadelphia, Pa., USA.
Dr. P. V. Marcussen, Physician in charge, Venereal Disease Clinic, Kommune-hospitalet, Copenhagen, Denmark; Chairman, WHO Syphilis Study Commission to the United States.
Dr. E. W. Thomas, Professor of Clinical Medicine, New York University College of Medicine; Director, Rapid Treatment Center, Bellevue Hospital, New York City, N. Y., USA.

Observers :

Dr. G. E. Samsme, Venereal Disease Consultant, Pan American Sanitary Bureau, Washington, D. C., USA
Dr. P. Sanchez, Chief, Venereal Disease Division, Department of Health, Caracas, Venezuela.
Dr. W. F. Snow, President, International Union against Venereal Diseases, New York City, N. Y., USA.
A. Woodchek, International Labour Office, Washington, D. C., USA.

Secretariat :

Dr. T. Guthe, Chief, Venereal Diseases Section, WHO (*Secretary*)
Dr. A. Spillmann, Regional Adviser on Venereal Diseases for Europe, WHO.
Dr. M. Grzybowski, Professor of Dermatology, Director, Clinic of Dermatology and Syphilology, University of Warsaw, Poland, was unable to attend.

several developments have made imperative a broader consideration of the entire group of treponematoses. Of these developments, most important is the evidence that the various treponematoses—syphilis, yaws, pinta, and bejel—respond to penicillin treatment. This seems to substantiate the hypothesis of Hudson that the treponemal diseases, including syphilis, are caused by closely related organisms but exhibit varying clinical and epidemiological patterns in different parts of the world, possibly because of environmental factors.

The success of mass application of penicillin in "eradication projects" against yaws and syphilis in parts of Africa, certain Pacific islands, and the USA has encouraged WHO support of the campaign against yaws which is part of the United Nations technical assistance to Haiti. The Expert Committee on Venereal Infections welcomed this project as an opportunity to demonstrate the effectiveness of control programmes based on penicillin in a large-scale campaign in a geographically delimited area with a high prevalence of disease. It recommended that procaine penicillin G in oil with 2% aluminium monostearate be the form of penicillin employed.

A second significant development is the treponemal antibody technique introduced by Nelson, which permits study of the biological and immunological relationship between the causative agent of the various treponematoses in man and animals, a distinction which cannot be made with classical serological method.

A third important technical consideration is the recent support given to the identification of bejel as an endemic syphilitic disease. The committee recommended that the bejel project in the Eastern Mediterranean area should get under way early in 1950. This project, proposed by the Director-General of WHO and adopted by the Regional Committee for the Eastern Mediterranean, calls, in the first place, for a survey to be carried out by a special team of 3 or 4 experts who would explore the epidemiological, clinical, laboratory aspects of bejel. Next would be the selection by this team of a special demonstration area where a disease-eradication campaign based on penicillin and modern case-finding techniques could be carried out. On the basis of experience gained in the demonstration area, it would be possible to proceed with a broad campaign against bejel over a wide area. Concomitant with the control programme would be comparative laboratory studies, particularly on the trepenomes of syphilis and bejel. It was the opinion of the Expert Committee on Venereal Infections that the pilot area for field and laboratory investigations should be established in Iraq as soon as the hot season is over.

It is felt WHO can make a significant contribution to the ultimate definition of the nature of treponemal diseases in man and of their biological and immunological relationships by utilizing the clinical and laboratory material available in field units and national laboratories in areas where treponematoses are prevalent. The disease-eradication campaigns against yaws and syphilis in Haiti and against bejel in the Eastern Mediterranean area will be a step in this direction.

Two considerations of an administrative nature were brought to the attention of the Expert Committee on Venereal Infections:

1. The referring of treponematoses other than syphilis to the Expert Committee on Venereal Infections by the Executive Board and the World Health Assembly.

2. The decision of the Second World Health Assembly to establish in 1950 an Expert Committee on Treponematoses, to be composed of 9 members, including 3 syphilis experts of the present Expert Committee on Venereal Infections. The latter recommended that the terms of reference of the new committee be clarified so as to avoid duplication of effort, or that WHO consider merging the two committees in 1951. Also recommended was the establishment of appropriate study-groups or subcommittees as required.

Serodiagnosis

Of major importance in any venereal-disease activity is to have uniform, effective, and practical means of serodiagnosis. At the present time there is little uniformity in the methods used, and comparisons of reactions are not always valid. The same method may give different reactions in the same patient because of differences in the material or in the technique employed. There are numerous other complicating factors, chief among which are:

1. Unreliability of test methods under different climatic conditions. Test methods which are reliable in temperate climates often fail under tropical conditions.

2. Impracticability of some of the most reliable techniques. Procedures which are very elaborate and expensive have limited use, particularly in mass screening activities under field conditions.

3. Limited manufacture of cardiolipin antigens. Technical difficulties and the patent protection for the production of cardiolipin lecithin make the wide use of this means of serodiagnosis very difficult at present.

Although the situation with regard to serodiagnosis is unsatisfactory, the committee did not want their observations to be taken as a complete invalidation of present methods. The problem becomes one of trying to

improve serodiagnostic methods. According to the committee, "the most promising development in this regard is the introduction of the immobilizing antibody technique (Nelson and Turner); . . . The differentiation between what appear to be true and non-specific reagins employing this technique may in future prove of fundamental importance in the serodiagnosis of syphilis".

The committee recommended that the Subcommittee on Serology and Laboratory Aspects, the report of which is discussed elsewhere in this issue, proceed with its programme for the establishment of an international antigen reference standard, study the possibility of recommending a uniform test procedure to all countries, and consider setting up international reference centres for making control sera and antigens available to national laboratories.

Antivenereal Drugs and Therapy

A survey recently made by WHO shows that penicillin consumption is likely to increase progressively in all parts of the world, whereas production will probably remain limited, for some time, to Europe and America. The Expert Committee on Venereal Infections considered this survey incomplete, however, and recommended that the study be continued.

The committee discussed the use of repository penicillin preparations, which have greatly simplified penicillin therapy. A single injection of 300,000 Oxford units of procaine penicillin with 2% aluminium monostearate can maintain an effective blood level for about 96 hours. Penicillin treatment in dosages of 600,000 to 2,400,000 units has special significance in cases of early infectious syphilis. The committee recommended that sufficient time has not yet passed to evaluate with certitude the ultimate results of this penicillin treatment. However, it is remarkable that, in observations made during the last two years, there do not appear to have occurred any completely acceptable instances of central nervous system relapse in patients who received adequate penicillin therapy in the early stages of infection. This gives hope that the danger of development of syphilis of the central nervous system may pass and that the prolonged post-treatment follow-up, which is presently necessary, may be curtailed and a shorter routine adopted.

Recognizing the epidemiological value of penicillin, the committee considered that its use on a large scale should be organized as part of public-health activities in areas with a high prevalence of treponemal disease. To compare its efficacy with older methods of treatment, a group of three members of the committee will report at a subsequent meeting on suitable case material treated with (*a*) arsenicals and/or bismuth, and (*b*) penicillin preparations.

With regard to the *Pharmacopoea Internationalis*, now being prepared by an expert committee of WHO, it was suggested that the characteristics of vehicles and water-repellent substances used in penicillin preparations be included in the *Pharmacopoea*. Standardization of repository preparations is essential if comparative investigations are to be valid. The committee also considered that the following drugs should be included in the *Pharmacopoea Internationalis*:

Arsenoxides
Aureomycin
Neoarsphenamine
Procaine penicillin G
Sodium penicillin G
Streptomycin
Sulfadiazinum
Sulfaguanidinum
Sulfathiazolum

Maritime Aspects

The committe made specific recommendations regarding these questions, calling attention to the desirability of more countries' adhering to the Brussels Agreement pending the establishment of wider international regulations for venereal-disease control and to the need for liaison with the Joint ILO/WHO Committee on the Hygiene of Seafarers.

Study Commission to USA

The committee expressed the opinion that the interim report of the WHO Syphilis Study Commission to the United States represents a significant contribution which many health administrations, institutions, and workers in the venereal-disease field will wish to have as a reference document. The results obtained by the Commission will be summarized in a forthcoming issue of the *Chronicle*. The report itself will be published Shortly as *World Health Organization: Technical Report Series*, no. 15.

Developments and Perspectives

In setting forth long-and short-term objectives for WHO's venereal-disease activities, the committee emphasized the following points:

1. Priority should be given to economically underdeveloped areas with a high prevalence of syphilis and/or other treponematoses.

2. WHO should continue its advisory and demonstration services and should stimulate traing of personnel in the field. The facilities in demonstration areas can be used effectively in training programmes.

3. Venereal-disease control activities should be integrated with other public-health programmes, particularly those relating to general disease prevention to maternal and child health. Pregnancy care provides an opportunity for case-finding not only among mothers but also among other members of families. Mass examinations for malaria and tuberculosis also

aid in finding cases. Antisyphilitic programmes should be combined with measures against other treponematoses where these are prevalent. An effort should be made to initiate activities which can continue to operate after outside assistance is withdrawn.

4. WHO should continue to assemble and distribute venereal-disease literature to health administrations and other institutions concerned. The rapidity of technical developments in the therapeutic and laboratory aspects of venereal-disease control make it difficult for research and field workers in all countries to be adequately informed. WHO's services as a clearing-house and distribution centre for venereal-disease literature have significant value.

Serology of Syphilis

The Subcommittee on Serology and Laboratory Aspects (of the Expert Committee on Venereal Diseases) devoted the major part of the discussions at its first session,* held in Washington from 12 to 20 October 1949, to the question of the International Serological Laboratory Conference which the World Health Organization proposes to convene in 1951 or 1952. Similar conferences took place in 1923 and 1928 at Copenhagen and in 1930 at Montevideo. The war prevented the holding of one in Copenhagen in 1939, as had been planned. In 1941 a conference for the Western hemisphere met in Washington. It was of great benefit to the subsequent development of research in the USA and laid the foundation for further standardization work in the serology of syphilis.

Need for an International Conference

The need to hold a new laboratory conference is making itself urgently felt. The facts, as was stressed by the subcommittee, that present techniques

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* The following took part in this session:

Members:

A. Harris, Senior Serologist, Venereal Disease Research Laboratory (US Public Health Service), Island, N.Y., USA

Dr. P. Krag, Assistant Director, Serodiagnostic Department, State Serum Institute, Copenhagen, Denmark (*Chairman*)

Dr R. Laporte, Chef du Service de la Serologie Institut Pasteur, Paris France

Dr I. N. Orpwood Price, Director, Venereal Diseases Reference Laboratory (Public Health Laboratory Service), St. Peter's Hospital, London, United Kingdom (*Vice-Chairman*)

Consultants and Advisers:

Dr P. V. Marcussen, Physician in charge, Venereal Disease Clinic, Kommunehospitalet, Copenhagen, Denmark

Dr T. B. Turner, Professor of Bacteriology, School of Hygiene and Public Health, Johns Hopkins University, Baltimore Md., USA

Dr M. V. Veldee, Medical Directory, Hyland Laboratories, Los Angeles, Cal., USA (Member of WHO Expert Committee on Biological Standardization)

Secretariat:

Dr T. Guthe, Chief, Venereal Diseases Section, WHO (*Secretary*)

Dr A. Spillmann, Regional Adviser on Venereal Diseases for Europe, WHO

for the serodiagnosis of syphilis lack uniformity; different methods of reporting the results of serological tests lead to confusion and render valueless many of the studies published in the past on the serology of syphilis. The present position is such that an individual may be declared syphilitic in one country and free from the disease in another.

There are, in addition, other factors emphasizing the need for an international serodiagnostic laboratory conference. New serological tests have been introduced into practice in the USA and elsewhere during recent years, but many countries have not yet tried them out. Some of these tests employ antigen components of a much higher degree of chemical purity than the ones previously used. This is particularly true in the case of antigens containing cardiolipin and purified lecithin, which have been found more sensitive and more specific than antigens prepared with less pure extracts. The advances made in this field open up the possibility of establishing a durable reference antigen standard. It is clear that developments of the greatest interest are possible in this direction.

Furthermore, a new method has been evolved which arouses great hopes among serologists, namely Nelson's treponemal antibody technique.[9] According to this technique, the serum of syphilitic rabbits and of persons in whom the disease has proceeded beyond the primary stage immobilizes virulent *Treponema pallidum* and causes it to lose its power of infecting the rabbit. This immobilization, which develops only in the presence of complement, appears to be due to a specific antibody which is different from and independent of the reagin detected in ordinary serological tests. As may be imagined, Nelson's technique opens up great possibilities in the immunology of syphilis. Moreover, as pointed out by the subcommittee, it could play an important part in the interpretation of false positive reactions.

Finally, there is an important reason, in addition to the above technical grounds, for organizing this conference on a world scale. Investigations so far made show that in certain areas, particularly in the tropics, seropositive reactions are extremely frequent; furthermore, the frequency varies according to the type of test used in serodiagnosis. It follows that the evaluation of the test and choice of reactions adapted to the various areas represent a problem which should be tackled on a world scale. Consequently, it will be necessary to obtain for the conference sera originating in different parts of the world. The subcommittee therefore appealed to all important laboratories to collaborate.

General Plans for the Conference

After unanimously recognizing the need for an international conference on serological techniques, the subcommittee took up the practical side

of its organization, which it discussed in its broad outlines. Various suggestions were examined concerning the date, place, number of participants, general programme of work, etc. In the view of the subcommittee, the conference should be convened in a city which is an important medical centre and which has an airport served by one or more world airlines, so as to ensure the transport of samples of sera coming from different parts of the world in the minimum time. Laboratories should be chosen so as to offer the best working conditions to the greatest possible number of authors of tests. London, Paris, or Copenhagen would fulfil these various conditions. The number of methods which would be demonstrated at the conference is estimated to be about 40. They should be selected on a purely technical basis, the demonstrations being given by the author of the method or by workers designated by him.

The subcommittee was of the opinion that tests should be run on at least 3,000 sera, at the rate of 200 a day, and on 250 samples of spinal fluid, at the rate of 16 per day.

The categories of sera with which the tests would deal would be the following :

Normal sera : About 1,500 samples taken from individuals not showing any morbid symptoms—but not a serologically pre-selected group—coming from at least three geographical areas.

Abnormal, non-syphilitic sera : About 500 samples taken from individuals suffering from malaria, leprosy, herpes genitalis, from patients who are febrile owing to disease, from pregnant women, etc. ; about 300 samples of sera giving false positive reactions and also complying with various definite conditions.

Syphilitic sera : About 1,000 samples taken from individuals suffering from primary, secondary, or tertiary syphilis of whom only a part have received appropriate treatment. The number of recent untreated cases should not be below 100.

Spinal fluid : Samples from subjects without syphilitic symptoms and from syphilitics in whom the central nervous system has not been affected.

National Centres for Serodiagnosis

Other problems dealt with during the session are also indirectly connected with the projected conference, particularly co-operation between laboratories or national centres in the reciprocal evaluation of performance of test and the exchange of information.

Samples of sera and antigens intended for serodiagnosis have already been exchanged between laboratories in Bulgaria, Denmark, Ethiopia, Finland, France, Italy, and the United Kingdom and the Venereal Disease

Research Laboratory of the US Public Health Service, which acted as reference centre. These exchanges were found to be so fruitful that they might well be established on a more systematic basis. This system should be extended to national laboratories in all WHO regions. Such exchanges of information between laboratories might also make useful contributions to the methods of conserving sera, particularly those which give false positive reactions; present knowledge on this subject is very limited.

The subcommittee suggested that WHO draw the attention of national health-administrations to the necessity of establishing in each country a laboratory or national centre for the serodiagnosis of syphilis to participate in action taken in this field on an international scale.

Other Questions

After having examined various questions relating to the projected conference, the subcommittee proceeded to deal with several other subjects. In particular, it studied the problem of cardiolipin, that of bejel and the other treponematoses, considered from the serological viewpoint, and the various problems raised by the technique of mass serological examinations.

Cardiolipin

The use of antigens based on cardiolipin-lecithin had been advocated by the Expert Committee on Venereal Diseases during its second session in an effort to encourage the standardization of serological tests for the diagnosis of syphilis.

There are two important obstacles to the general use of cardiolipin: the technical difficulties encountered in large scale production of this substance and the fact that its manufacture is protected by a patent. The latter, which is held by the New York State Department of Health, was established not for commercial purposes, but to ensure the purity of the cardiolipin products. It has been suggested that WHO administer this patent internationally. The subcommittee considered that, if the administration of international patents were not within the province of WHO, the problem could be approached in another way: the possibility of establishing an international cardiolipin reference standard might be considered in conjunction with the Expert Committee on Biological Standardization, should developments in this field indicate this to be advisable. A high degree of purity of cardiolipin is essential to ensure the accuracy of serological tests employing antigens containing cardiolipin and purified lecithin. Consequently, the current purity control tests for this substance should be studied by the subcommittee.

Bejel, syphilis, and other treponematoses

Thanks to technical improvements made during the last two years, it is now possible to obtain sufficiently concentrated and pure suspensions of

treponemata, i.e., without tissular impurities, for the study of various serological problems connected with the immunology of syphilis, false positive reactions, and the relationships, both biological and immunological, between the various strains of treponemata. The members of the subcommittee had an opportunity, thanks to the courtesy of the Department of Bacteriology, Johns Hopkins School of hygiene and Public Health, Baltimore, to become acquainted with research on treponemal antibodies and particularly with the new treponemal antibody technique.

Several interesting points were brought to light by the comparative study of the different techniques.

The titre of the immobilizing antibody (Nelson's antibody) is generally high in syphilis; at times it is distinctly at variance with the reagin titres obtained by the lipoid antigen method. After specific treatment, the Nelson antibody persists longer than the reagin. Finally, there is the particularly striking fact that the Nelson test has been consistently negative in all cases of undeniably false positive reactions. Furthermore, the Nelson technique has made it possible to differentiate strains of *T. pallidum* and *T. pertenue*.

These results promise developments of the greatest interest. On the one hand, as pointed out by the subcommittee, the treponemal antibody technique enables a different approach to be made to the study of false positive reactions and perhaps to elucidate their nature. On the other hand, it may make it possible to study the various strains of treponemata with reference to their biological and immunological inter-relationships.

The programme for the control of bejel will enable interesting experiments in this field to be made in the near future. This WHO project for a campaign against bejel in the Eastern Mediterranean region, where this disease represents an important public-health problem, met with the approval of the subcommittee. From the serological viewpoint, various investigations could be undertaken in which the new techniques would play a part. The results obtained would increase present knowledge of bejel and throw light on the problem of the other treponematoses. These studies would be concerned with the following points:

(a) serological relationship between bejel and syphilis;

(b) nature and extent of bejel;

(c) experimental infection of the rabbit with the bejel treponema;

(d) immunity and cross-immunity in experimental treponematoses (syphilis, pinta, yaws, bejel).

Mass serological examinations

The general application of mass serological examinations has shown the acute nature of certain serological problems, such as false reations –both positive and negative–the drawbacks attached to the use of a single

test for diagnosis, etc. To these technical questions are added problems of a practical nature, e.g., pressure of work in laboratories which have to carry out thousands of flocculation or complement-fixation tests daily, the inadequate equipment of laboratories in underdeveloped areas, etc.

The subcommittee noted various practical experiences, particularly the satisfactory results obtained by the WHO venereal-disease demonstration team at Simla in Northern India with a modified Meinicke test, used in conjunction with a cardiolipin test.

On the basis of this preliminary information, the subcommittee recommended that techniques suitable for mass examinations be studied and that the results and the statistical data collected by the demonstration teams be assembled and submitted to the subcommittee at its next session.

Chr. W.H.O. IV: 35-45, Feb. '50.

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Hind Kusht Nivaran Sangh

It is proposed to hold the next Leprosy Training Course at the School of Tropical Medicine, Calcutta, from 16th August to 16th September 1950 both days inclusive, provided sufficient number of candidates is forthcoming. The selection of candidates will be made by Dr. Dharmendra, Officer in charge, Leprosy Research Department, School of Tropical Medicine, Calcutta. It is therefore requested that names of candidates may be submitted direct to him which should reach him by the 15th July, 1950.

The value of the course would be greatly enhanced if officers of the senior grade are sent up for training. It is therefore requested that doctors of the senior grade, who have special aptitude for leprosy work, should be nominated. The syllabus for the course can be had from the Department.

No registration fee will be charged from candidates attending the course. Their travelling expenses should, as usual, be met either by the State Branches concerned or by the doctors themselves or their employers.

* * * * *

From our Book Shelf

THE COMMON DISEASES OF THE SKIN :—By R Cranston Low, M. D., F. R. C. P. E., F. R. S. E. and G. A. Grant Peterkin, M. B. E. M. B. F. R. C. P. Ed., Fourth Edition, 1945. Published by Oliver & Boyd, 18, chapters, 280 pages, 148 illustrations.

The diseases of the skin form an important aspect of the general practice and the general practitioner often finds it difficult to diagnose and to treat them effectively. The book is aptly written to guide and help the practitioner in dealing with the common skin affections as met with in his daily practice.

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The book is immensely useful to the general parctitioner and senior medical students and deserves to be kept permanently in the medical library of every doctor.

The language is simple and lucid and the illustrations are of high order. The paper, printing and binding are excellent and attractive.

L. G. B.

Indian Journal of Venereal Diseases & Dermatology

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Edited by Dr. U. B. Narayanrao (Editor, "Medical Digest" and Member, Medical Council, Bombay).

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